REMARKS

Claims 25 and 26 are pending in the application. Claim 26 is rejected under 35 U.S.C. § 112, first paragraph. Claims 25 and 26 are rejected under 35 U.S.C. § 102(b). Applicants request reconsideration and withdrawal of the rejections in view of the reasons set forth herein.

I. The Rejection of Claim 26 Under 35 U.S.C. §112, first paragraph

Applicants can not understand the rejection under §112 because a rejection is not presented in the Office Action. Applicant's note that the sentence "When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation" (See Office Action page 3, last sentence of the first paragraph) is not an actionable rejection under the statutes. It is not the Examiner's position that is relevant, it's the Examiner's reasoning. Absent specific factors and a reasoned statement as to exactly why one skilled in the art could not practice the invention, the rejection must be withdrawn.

To summarize the Examiner's rejection under §112, it was urged that the claims contain subject matter that is not described in the specification in such a way as to enable one skilled in the art to make and use the invention. The Examiner then generally referred to factors set forth in In re Wands, and simply stated the position that one skilled in the art could not practice the invention.

The In re Wands factors were then listed, as follows.

(1) The Nature of the Invention - The Examiner simply indicates that the invention was directed to a method of treating well-known diseases which routinely occur in the population. Nothing under this factor can be interpreted as requiring undue experimentation.

(2) The State of the Art - It is noted that the diseases treated under the invention are currently treated by known medicaments. Nothing under this factor can be interpreted as requiring undue experimentation.

Moreover, applicants note that one of the medicaments known to treat these diseases is paroxetine. As indicated in claims 1 and 4 of United States Patent No. 6,133,289 ('289), paroxetine has been indicated in the treatment of the disease states of claim 26. A copy of the '289 patent is enclosed herewith for the convenience of the Examiner. The '289 patent is not being submitted under the duty of disclosure so a Form PTO 1449 is not being submitted herewith.

(3) The Relative Skill in the Art - The relative skill in the art is indicated as "high". It is stated that it is not uncommon for scientists to have the level of Ph.D. of education. But no further elaboration or reasoning is included under this factor as to why the claimed invention is considered to require undue experimentation.

There are no standard rejections under §112 for inventions directed to technology areas where the level of skill is considered "high". Even though the level of skill is considered "high" by the Examiner, there are more than a sufficient number of "highly" skilled workers in the pharmaceutical industry to successfully develop the instant technology. Indeed, the vast majority of inventors on pharmaceutical patents have a Ph.D. Absent any reasoned statements by the Examiner, nothing under this factor can be interpreted as requiring undue experimentation.

(4) The Predictability or Unpredictability of the Art - Contrary to the Relative Skill in the Art, the Examiner considers the unpredictability of the drug dosage art to be only "fairly high". Again, there is no further elaboration or reasoning included under this factor as to why the claimed invention is considered to require undue experimentation.

Applicants submit that the "highly skilled" workers of the pharmaceutical industry (especially those who have earned a Ph.D.) are more then qualified to work in the drug dosage art where the level of skill is only "fairly high".

Moreover, the pharmaceutical arts is a well established technology area and, even though the level of skill in the drug dosage art may be "fairly high", it is considered a matter of routine for the skilled pharmaceutical worker to determine an effective dose of a pharmaceutically active compound. Further, as indicated by claims 1 and 4 of the '289

patent, the use of paroxetine in treating the instant diseases has already been acknowledged by the Patent and Trademark Office.

Absent any reasoned statements by the Examiner, nothing under this factor can be interpreted as requiring undue experimentation.

(5) The Breath of the Claims - There are three sentences under this factor. 1 - The claims are considered "very broad". 2- The claims are considered to permit any oral paroxetine formulations that comprise enteric coatings. 3 - WIPO 92/09281 is cited as describing formulations comprising paroxetine that are both slow release and enteric coated.

Regarding the fist and second sentences, applicants state the following.

In stating that the claims permit any oral paroxetine formulations that comprise enteric coatings, the Examiner is wrong . The claims require that the formulations be both controlled and delayed. Enteric coatings only delay the release of the active. Once the enteric coating is spent, the active is immediately released. And not controlled released as in the claimed invention.

As indicated on page 1 of the specification (lines 22 to 30), controlled release means a formulation in which the active is released at a slower rate than from a conventional immediate release product and delayed release means the active is released at a later time than from a conventional immediate release product. Because applicant's invention requires that the formulation be both controlled and delayed, the formulations of the invention release the active at a later time than an immediate release formulation and, after the delayed release aspect is spent, the remaining formulation releases the active at a slower rate than an immediate release formulation. As such, applicant's invention is directed to a very specific kind of formulation, one that is both controlled and delayed. The claims are not "very broad", as urged by the Examiner.

Moreover, the claims do not permit any oral paroxetine formulation that comprises enteric coatings, as urged by the Examiner. Applicants specifically request that the Examiner explain how an enteric coating over an immediate release oral formulation containing paroxetine could be covered by the instant claims.

Regarding the third sentence, wherein WIPO 92/09281 is cited as describing formulations comprising paroxetine, applicants note that the rejection here is under § 112, for enablement. Applicant's request that the Examiner explain the relevance of citing a reference that allegedly describes the invention to the issues of whether one skilled the art could practice the invention. Applicants contend that the citation of WIPO 92/09281 is not pertinent to the issue of eablement and do not further address the issue here.

Additionally, applicants note that claim 26 is also rejected under § 102. In order for a reference to anticipate an invention, the reference must sufficiently describe the claimed invention to have placed the public in possession of it. *Minnesota Mining & Mfg.* v. *Johnson & Johnson Orthopedics, Inc.* 24 USPQ2d 1321. It is inconsistent for claim 26 to be rejected under § 112 because it would require undue experimentation on the part of the public to arrive at the invention, and at the same time rejected under § 102 because the public is already in possession of the invention.

Applicants request that the Examiner explain how claim 26 can be rejected under § 112 and § 102.

In Summary

Applicants contend that a proper rejection under § 112 has not been made because the Examiner failed to state specific factors and a reasoned statement as to exactly why one skilled in the art could not practice the invention.

In view of the '289 patent, the use of paroxetine in treating the instant diseases has already been acknowledged by the Patent and Trademark Office.

Applicants specifically request that the Examiner state for the record the following.

1 - How an enteric coating over an immediate release oral formulation containing paroxetine could be covered by the instant claims.

2 - Explain the relevance of citing a reference that allegedly describes the invention (Specifically WIPO 92/09281) to the issues of whether one skilled the art could practice the invention.

3 - How claim 26 can be rejected under § 112 and § 102.

II. The Rejection of Claims 25 and 26 Under 35 U.S.C. §102(b)

Claims 25 and 26 are directed to a pharmaceutical formulation that combines two technologies. The formulation is both controlled and delayed. As indicated on page 1 of the specification (lines 22 to 30), controlled release means a formulation in which the active is released at a slower rate than from a conventional immediate release product and delayed release means the active is released at a later time than from a conventional immediate release product. Because applicant's invention requires that the formulation be both controlled and delayed, the formulation of the invention releases the active at a later time than an immediate release formulation and, after the delayed release aspect is spent, the remaining formulation releases the active at a slower rate than an immediate release formulation.

Claims 25 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Johnson. Johnson is indicated as teaching formulations of paroxetine, including slow release methods or enteric coated tablets, in the treatment of bulimia and anorexia.

In explaining the rejection, the Examiner states (on page 4, last half sentence on the page) "Johnson teach that the paroxetine preparation may be formulated for administration **by any route**..." (Emphasis added) and (on page 5, last sentence of the first half paragraph on the page), "The tablets may be coated (e.g. enteric coated tablets) according to methods well known in the pharmaceutical practice and **may, if desired,** be designed to give slow release of paroxetine."(Emphasis added)

Applicants note that the courts and PTO practice does not equate broad disclosures and statements such as "by any route" with destroying the novelty of every permutation under the broad disclosure or statement. And a reference that, at most,

suggest the claimed combination "**may, if desired,** be designed" falls far short of the statutory requirements for anticipation under §102.

In order to be anticipating, a reference must sufficiently describe the claimed invention to have placed the public in possession of it. *Minnesota Mining & Mfg. Co.* v. *Johnson & Johnson Orthopedics, Inc.*, 24 U.S.P.Q2nd. 1321 [hereinafter 3M]. The reference must clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without the need for picking and choosing. *In re Arkley* 172 U.S.P.Q 524. The reference must therefore provide a degree of precision with respect to the specific invention claimed.

For example, in *Ex parte Westphal*, 223 U.S.P.Q. 630, the claim was directed to a composition containing 3-methylthio-4-amino-6-tert-butyl-1,2,4-triazine-5-one. The Examiner rejected the claim under §102 as anticipated by, *inter alia*, a patent to Fawzi. This patent disclosed a compound substituted at a particular position with alkyl having 1 to 8 carbon atoms, but did not specifically name the claimed tert-butyl radical. Thus, the Board found that the Fawzi patent did not provide the precision necessary for anticipation under §102.

Similarly, in *Arkley*, the court found that the single claimed compound was not described in the prior art within the meaning of §102. The prior art generically disclosed a class of compounds encompassing the claimed compound, as well as over 230,000 other compounds. The Board contended, however, that the prior art contained two examples that disclosed the exact precursors of the claimed compound. The court found that these examples disclosed exact precursors only to the extent that one selects the correct acid to react with a particular tertiary amine, which also must be selected. The court further found that there was nothing in the reference that clearly and unequivocally directs those skilled in the art to make this selection. Thus, the court reversed the rejection under §102.

Johnson is a second medical use application, not a formulation application. The compound used in Johnson is paroxetine. Part of the disclosure of this application indicates that the compound can be administered by any route. Further, in distant parts of

Johnson, among a myriad of formulation possibilities, administration by enteric coated formulation and slow release formulation are separately mentioned. And, there is no teaching or suggestion in the application to combine any of the separately listed formulation possibilities.

Because Johnson fails to teach or suggest a pharmaceutical formulation that is both controlled and delayed, Johnson fails to place the instant invention in the possession of the public [3M]. Because Johnson merely lists enteric coatings and slow release among a vast number of formulation possibilities under the catch-all term **by any route**, Johnson fails to clearly and unequivocally direct those skilled in the art to make the selection of applicant's invention. [*Arkley*] Because Johnson does not name a single formulation that is both controlled and delayed but at most suggest that combinations **may, if desired,** be designed, Johnson does not provide the precision necessary for anticipation under §102. [*Ex parte Westphal*].

Applicants wish to take issue with a number of statements made by the Examiner in the Response to Arguments section.

First, on the top of page 6, first full sentence, the Examiner states "There is no significant distinction observed between the instant invention and the prior art since the prior art teaches.....various release forms, such as enteric coated tablets and slow release dosage forms, which are functionally equivalent to delayed and controlled forms, **respectively**." (Emphasis added). Here the Examiner fails indicate any awareness that applicant's invention combines two technologies. Applicant's invention is directed to a very specific pharmaceutical formulation, one that is both controlled and delayed. The effect of a controlled formulation alone and a separate delayed formulation respectively is simply not germane to a patentability analysis of the present invention.

Second, on page 6, in the last two sentences of the top half paragraph, the Examiner states: "Johnson teaches the generic concept of formulating both slow and enteric release dosage form comprising paroxetine as the active ingredient." (Emphasis

added) "Therefor the instant invention is rendered unpatentable over the prior art." This passage shows that the Examiner's rejection under §102 is predicated upon a generic concept of two individual technologies selected from numerous disclosed possibilities with the benefit of hindsight from applicant's invention. And where the prior art does not even suggest that the recited individual technologies could be combined.

To establish anticipation, the law requires identity between the claimed invention and the prior art disclosure. *Kalman v. Kimberly-Clark Corp.*, 218 U.S.P.Q2nd 781. A rejection based upon a generic concept falls far short of the statutory requirements for anticipation under §102.

Applicants specifically request that the Examiner explain the above passages. Did the Examiner fail to realize that applicant's invention was directed to a single formulation that combined two formulation technologies, controlled and delayed? Or does the Examiner believe that a rejection under §102 can be maintained on an invention directed to a combination of specific technologies, where the prior art simply provides a broad list of individual technologies with no motivation to combine them? Does the Examiner believe that a generic concept is sufficient to destroy the novelty of all permutations that fall within that generic concept?

Applicants specifically request that the Examiner state for the record where the Examiner found the motivation to combine the separately listed technologies in Johnson. One skilled in the art, in view of Johnson, would conclude that there is no need to combine the technologies, as the suitable formulations were already listed.

Third, on page 6 third to the last sentence of the first half paragraph, the Examiner states "Furthermore, there are no unexpected results that accrue from the use of applicant's instant release forms."

Applicants have continuously maintained throughout the prosecution of this application, and its parent (now United States Patent No. 6,548,084), that applicants' disclosed advantage of a reduction in the incidence of nausea and vomiting is a beneficial and unexpected result of the

instant invention. At the time of applicant's invention, selective serotonin reuptake inhibiting compounds were known to cause nausea and vomiting. Further, these compounds were known to act in the central nervous system (CNS). It is a surprising and unexpected discovery to find that by changing the formulation (and thereby the point of absorption in the gut) a side effect thought to be centrally mediated could be alleviated. Such improvement is indeed beneficial and unexpected.

The Examiner appears to equate the utility of treating anorexia and bulimia with paroxetine with a reduction in the incidence of nausea and vomiting. This analysis is wrong. Johnson discloses that paroxetine may be used to treat bulimia and anorexia. Bulimia and anorexia are not associated with nausea. To the extent that bulimia and anorexia are associated with vomiting, this vomiting is self induced in order to negate excessive calorific intake caused by binge eating (bulimia) or to achieve weight loss (anorexia). It is not nausea and vomiting as a side effect of paroxetine administration. Because Johnson does not contemplate or address applicants problem, Johnson can not anticipate or render obvious applicants solution.

To put it simply, bulimia and anorexia are disorders of the central nervous system, not the gut. As indicated above, the unexpected advantage of a reduction in nausea and vomiting in the administration of paroxetine is related to the rate and location of drug deposition in the gut. There is marginal benefit to the use of a medicament in treating a disease state in which a symptom is vomiting, when the medicament itself makes you vomit. The fact that the instant invention reduces the nausea and vomiting associated with the administration of paroxetine is an unexpected and beneficial improvement in the treatment of any disease state, including anorexia and bulimia.

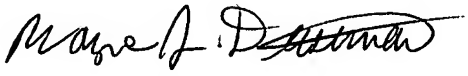
Examiner indicates no awareness of applicants unexpected and beneficial effects (or, for some reason, even the existence of the statements in the application or in previous responses).

Applicants specifically request that the Examiner state for the record why their disclosed unexpected and beneficial improvements regarding effects on the gut upon administering paroxetine, is not novel and patentable over the disclosure in Johnson.

Applicants contend that nothing in Johnson anticipates or renders obvious their invention as currently claimed. Applicants respectfully request that the rejection here be withdrawn.

Applicants therefore submit that all reasons for rejection have been addressed and that the currently pending claims are allowable. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number indicated below.

Respectfully submitted,



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